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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/552,324 | 10/07/2005 | Hans Loibner | 4518-0111PUS1 | 8937 |

2292 7590 09/18/2009

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

| EXAMINER | |
|---|---|
| BRISTOL, LYNN ANNE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1643 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 09/18/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/552,324 | LOIBNER ET AL. | |
| | Examiner | Art Unit | |
| | LYNN BRISTOL | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-10 and 12-34* is/are pending in the application.

4a) Of the above claim(s) *4,6-8,10,14-28 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 9, 12, 13, 29-32 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/2/09 has been entered.

2. Claims 1-10 and 12-34 are all the pending claims for this application.

3. Claims 1-3, 5, 9, 13, 31 and 32 are amended and new Claim 34 was added by amendment in the Response of 3/2/09.

4. Claims 4, 6-8, 10, 14-28 and 33 are withdrawn from examination.

5. Claims 1-3, 5, 9, 12, 13, 29-32 and 34 are all the pending claims under examination with species for a carbohydrate antigen (Lewis-Y, Sialyl-Tn and Globo H).

6. This Office Action contains new grounds for rejection.

***Withdrawal of Objections***

***Specification/ New Matter***

7. The objection to Applicants' amendment to the specification to cross-reference the instant application to the foreign priority application as an incorporation by reference for introducing new matter is withdrawn.

Applicants have amended the specification in the Response of 3/2/09 to delete the incorporation by reference phrase.

***Claim Objections***

8. The objection to Claims 31 and 32 for reciting an apparent typographical error is withdrawn in view of the amendment of both claims to recite "Globo H."

***Withdrawal of Rejections***

***Claim Rejections - 35 USC § 112, second paragraph***

9. The rejection of Claims 2, 3, 5, 29 and 30 for the recitation ""or fragments thereof" in Claims 2 and 3 is withdrawn.

Applicants have amended Claims 2 and 3 in the Response of 3/2/09 to clarify that the fragment corresponds to the tumor associated antigen.

10. The rejection of Claim 13 for the recitation "monoclonal antibodies produced by ATCC HB 9324 or ATCC HB 9347" because it is unclear how an antibody can be produced from an ATCC accession no. is withdrawn.

Applicants have amended Claim 13 in the Response of 3/2/09 to clarify that the antibodies are produced by hybridomas deposited under the recited ATCC accession nos.

11. The rejection of Claims 1-3, 5, 9, 13, and 29-32 for the recitation "wherein a constant region of said IgG1 antibody comprises a constant region of an IgG2a subtype amino acid" in Claim 1 is withdrawn.

Applicants have amended Claim 13 in the Response of 3/2/09 to clarify that the "IgG1 antibody comprises a constant region of an IgG2a subtype amino acid sequence."

***Claim Rejections - 35 USC § 112, first paragraph***

***Biological Deposit***

12. The rejection of Claim 13 under 35 U.S.C. § 112, first paragraph, because the specification does not provide evidence that the claimed hybridoma cell lines (HB 9324 and HB 9347) are (a) known and readily available to the public; (b) reproducible from the written description is withdrawn.

Applicants have provided copies of the deposit/accession no. information for each of the hybridomas obtained from the ATCC website in the Response of 3/2/09.

***Rejections Maintained***

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

## *Enablement*

13. The rejection of Claims 1-3, 5, 9, 12, 13, and 29-32 under 35 U.S.C. 112, first paragraph, is maintained because the specification does not reasonably provide enablement for introducing any fragment of the constant region from an IgG2 antibody into the constant region of any IgG1 antibody in order to obtain a constant region comprising any hamster or primate glycosylation and being immunogenic in any primate.

For purposes of review, the rejection was set forth in the Office Action of 9/2/08 as follows:

"***Nature of the Invention***

The claims encompass antibodies comprising any IgG2a subtype region from the constant domain cloned into the constant region an IgG1 antibody where the IgG2a comprises a hamster or primate glycosylation and the resultant recombinant antibody is designed for immunizing primates.

***Disclosure in the Specification***

The specification makes a general disclosure for anti-idiotypic antibodies against Lewis-Y (pp. 5, 12, 13, 14 and 36), Sialyl-Tn (p. 12) or Globo H (p. 12) carbohydrate antigens. The specification discloses an anti-idiotypic antibody for the Lewis-Y antigen in Example 8 where the recombinant IgG2a Le-Y antibody is an IgG2a hybrid designed for primate vaccination, which combines an anti-idiotyic Lewis-Y mimicking herpervariable region and the highly immunogenic mouse IgG2a constant regions as shown in Figure 4. The immunogenicity is reported to be improved over the parent antibody, IGN301 wherein the anti-idiotypic antibody produces a strong IgG response against Lewis-Y expressing epithelial cancer cells. The antibody is expressed in HEK293 cells, transformed human embryonic kidney cell cultures so would result in primate glycosylation.

It is not well established in the art that an antibody encompassed by the claims is amenable to the extent and degree of the modifications to the Fc or constant domain that would allow proper folding and assembly of the antibody, and the specification is not any more enabling for producing a functional, immunogenic antibody that meets all of the claim limitations.

***Prior Art Status: glycosylation of antibodies is unpredictable, dependent on the cell type and can affect antibody function.***

It is known that not all cells glycosylate proteins in the same manner. As evidenced by Wright et al (Springer Semin Immunopathology ,15 :259-273 (1993)), while N-linked glycosylation is a wide spread post translational modification, occurring among mammalian, yeast, insect and plant cells, "the processing steps in the Golgi apparatus vary among cell types". (Page 259, second paragraph). Wright documents that plant cells use xylose, mammalian cells use sialic acid, and yeast add many more mannose monomers than mammalian cells. Also insect cells do not appear to process the carbohydrates beyond the Man3 GLC Nac2 step. Accordingly, one skilled in the art would reasonably conclude that the tertiary structure of glycosylated antibodies, if actually glycosylated, which are encompassed by the broadly written claims would differ, based upon the teachings of Wright et al.

Further, Wright et al specifically teach that "the position of the carbohydrate addition appears to influence the structure of the added carbohydrate" (page 269, first full paragraph) and that "glycosylation can induce structural abnormalities in the light chain that lead to tissue deposition" (page 266-267, bridging paragraph). Finally, Wright et al

teach that the sugars may fill “pockets" within the immunoglobulin , thus one of ordinary skill in the art would reasonably conclude that addition of carbohydrates to an antibody would alter the tertiary structure as evidenced from Delente (Trends in Biotechnology 3, letters to editor, No.9, (1985)) which teaches each glycosylated protein must be evaluated individually to determine the importance of glycosylation to its function and stability. Thus Wright et al teach the unpredictability of adding a glycosylation site to an antibody molecule, specifically that some additions result in protein aggregation; that the position of the addition is important for determining whether the glycosylation site is in fact recognized by the cell; and once glycosylated, whether the antibody is more or less stable and binds antigen like the unaltered form. One skilled in the art would also reasonably conclude from Wright et al that glycosylation in the CH1 or constant K (CK) region could have similar structural effects as those in the light chain mentioned above.

As evidenced by Olden et al (Biochem et Biophys Acta 650:209-232 (1982)), carbohydrate structures are a form of sorting signals used by the cells and that O-linked glycosylation differ from N-linked glycosylation due to the sugars which are added to each type during protein processing. O-linked carbohydrates use galNAC while N-linked carbohydrates use GlcNAC (see page 225, second column, first paragraph). Olden teaches that O-linked carbohydrates differ in tertiary structure from N-linked carbohydrates and therefore, one skilled in the art would reasonably conclude that antibodies possessing O-linked sugars would also differ in their tertiary structure from those antibodies expressing N-linked sugars.

Moreover, while the N-linked carbohydrate addition site is specifically the sequence “ASP-X-SER/THR, where X may stand for any amino acid, the O-linked addition site is less defined as only a serine or a threonine residue. Carbohydrate moieties are not attached to all lumenal serine or threonine residues and it would be unpredictable to determine at which lumenal positions a serine or a threonine could be placed within the antibody molecule so that the serine or threonine would be glycosylated. Once glycosylated, whether by the N-linked or O-linked mechanism, it would require undue experimentation to determine whether the antibody expression, stability, tertiary structure or affinity had been affected.

Since the state of the art of protein modification suggests that the effects of sequence alterations are unpredictable, and furthermore, as evidenced by Wright et al, Delente, and Olden et al concerning the unpredictability of adding carbohydrates to antibodies and since the specification provides inadequate guidance as to which constant domain changes would result in hamster or primate glycosylation and a functional antibody, wherein the glycosylation site is actually used, and the antibody stability/function is not reduced, undue experimentation would be required to determine which IgG2 constant domain regions would result in the hamster- or primate-glycosylated antibody molecule that could still be bind its antigen and would be used to immunize primates.

***Prior Art Status: Modifications to the Heavy Chain Constant Regions are Unpredictable***

The claims encompass antibodies comprising modified constant regions and are not limited to the domain substitutions. The claims do not specify whether the hinge, CH1, CH2 or CH3 domains are substituted or where the substitutions would take place. It is well accepted in the art that the constant region contributes to flexibility, half-life and the effector functions of an antibody.

Salfeld (Nature Biotech. 25(12): 1369-1372 (2007)) describes some of the properties for the IgG isotype constant regions in Table 1 and suggests that the constant region can be modified based on the intended effector functions but that results can vary depending on which domain and how the domain is mutagenized (p. 1371, Col. 2, ¶2-3).

The state of the art at the time the invention was made recognized that even single amino acid differences can result in drastically altered function of antibodies. For example, Lund et al. (The Journal of Immunology 1996, 157:4963-4969) show that even a single amino acid replacement within the CH2 domain of IgG can alter the glycosylation profile of an antibody therefore influence its effector functions of Fc receptor binding and complement activation (see entire document, particularly Discussion on pages 4966-4968). Further, Lazar et al. (WO 03/074679) teach that the determinants of antibody properties, such as stability, solubility and affinity for antigen, important to its functions are overlapping; thus engineering an Fc region of an antibody may cause a loss in affinity for its antigen (see entire document, particularly page 3).

Given the extensive variation permitted by the instant claim language, the skilled artisan would not reasonably predict the combination of which IgG2 constant domain region, for example, CH1, hinge, CH2, CH3, and CH4 much less the CL have the same function as the instant claimed invention. Reasonable correlation must exist between the scope of the claims and scope to enablement set forth.

The specification does not appear to provide sufficient guidance as to which constant domains should or should not be changed to preserve any particular function. The variation permitted by the instant claim language is extensive. There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the claimed recombinant antibody.

Therefore, in view of the lack of guidance in the specification and in view of the unpredictability in the art of glycosylation of proteins as evidenced by Wright et al, Olden et al, and Delente and the unpredictability of glycosylation of antibodies as evidenced by the specification, one of skill in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Applicants' allegations on pp. 8-9 of the Response of 3/2/09 have been considered and are not found persuasive.

a) Applicants allege page 12, lines 10-16 of the Specification discloses that the antibodies of the invention are coupled to a carbohydrate residue, and therefore adding a glycosylation site at any position on the antibody would not lead to protein aggregation or improper folding of the antibody.

Response to Arguments

Pursuant to MPEP 2144.03, "ordinarily there must be some form of evidence in the record to support an assertion of common knowledge." Applicants' attorney assertions are not substantiated by extrinsic evidence in the form of experimental data or reference art. Applicants have not shown the genus for a usable product obtained from any carbohydrate molecule coupled to any amino acid in the constant region of any IgG1 antibody and where the constant region has been further modified to contain any sequence from the constant region of any IgG2a subtype. Applicants have not shown a structure/function correlation for the genus of antibodies that meet the structural and functional requirements of the instant claims.

Secondly, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed immunogenic antibody in a manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions, or substitutions to the constant region of the IgG1 antibody and comprising a IgG2a subtype much less any number of carbohydrate molecules being coupled anywhere within the constant region of the acceptor antibody constant region.

The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the protein's structure and still maintain biological activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F,2d 1200, 18 USPQ 1016 (Fed. Cir. 1991) at 18 USPQ 1026 1027 and Ex parte Forman, 230 USPQ 546 (BPAI 1986).

Finally, the examiner cited numerous references regarding the unpredictability of glycosylating antibody molecules with respect to their folding properties in addition to the unpredictability of modifying the constant regions of an antibody further with respect to their folding in the Office Action of 9/2/08; however, in the Response of 3/2/09, Applicants fail to address this highly pertinent aspect of the rejection for this field of art and which effectively rebuts Applicant's position.

b) Applicants allege the Specification discloses that the antibody may have a murine amino acid sequence or any other mammalian amino acid sequence that is combined with the murine IgG2a part. (Specification, page 9, paragraph 4). The Specification indicates that the preferred location of the IgG2a sequences in a hybrid antibody is in any one of the CL, CH1, hinge, CH2, and CH3 regions, though the hinge region is most preferred. (Specification, page 14, paragraph 2), and therefore, adding the IgG2a sequence to in the antibody would not affect the resultant hybrid antibody's stability, binding, and functionality. Additionally, a fully functional antibody, having two heavy chains and two light chains is not necessary to raise an immune response

against the antibody, because the invention uses the antibodies as a "carrier" to deliver an antigen mimetic and/or immunogenic glycosylation.

Response to Arguments

In response to applicant's argument that the antibody base or structure is merely "a carrier" with which to present an epitope or mimotope for a tumor associated antigen, it is noted that the features upon which applicant relies (i.e., the antibody is a carrier) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Additionally, the specification defines the term "immunogenic antibody" as:

> "An immunogenic antibody according to the invention may *have immunogenicity by its specificity or by its structure*. The immunogenic antibody can induce immunogenicity also when being denatured or when conjugated to certain structures or carriers" (p. 8, ¶6).

Accordingly, the antibody of the instant claims would then embrace an antibody having "specificity" for an antigen, which would seemingly require the antibody have a function for recognizing and binding antigen. It is not clear how the claimed antibody escapes the requirement of having VH and VL CDRs in view of the definition for an "immunogenic antibody" and the open language for the instant claims.

Finally, Applicants' assertion that "adding the IgG2a sequence to in the antibody would not affect the resultant hybrid antibody's stability, binding, and functionality" is not substantiated by documentation (see ) and is rebutted by the examiner's citation of the art references in the Office Action of 9/2/08.

The rejection is maintained.

## ***New Grounds for Rejection***

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### *Written Description*

14. Claims 1-3, 5, 9, 12, 13, and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass antibodies comprising any IgG2a subtype region from the constant domain cloned into the constant region an IgG1 antibody where the IgG2a comprises a hamster or primate glycosylation and the resultant recombinant antibody is designed for immunizing primates. Additionally, according to the definition in the specification an "immunogenic antibody" "may have immunogenicity by its specificity or by its structure. The immunogenic antibody can induce immunogenicity also when being denatured or when conjugated to certain structures or carriers" (p. 8, ¶6)."

Under the Written Description Guidelines (66 FR 1099 (Jan. 5, 2001); 1242 O.G. 168 (Jan. 30, 2001) revised training materials Mar 25, 2008), the claimed invention must

meet the following criteria as set forth.

a) Actual reduction to practice: The specification makes a general disclosure for anti-idiotypic antibodies against Lewis-Y (pp. 5, 12, 13, 14 and 36), Sialyl-Tn (p. 12) or Globo H (p. 12) carbohydrate antigens. The specification discloses an anti-idiotypic antibody for the Lewis-Y antigen in Example 8 where the recombinant IgG2a Le-Y antibody is an IgG2a hybrid designed for primate vaccination, which combines an anti-idiotyic Lewis-Y mimicking herpervariable region and the highly immunogenic mouse IgG2a constant regions as shown in Figure 4. The immunogenicity is reported to be improved over the parent antibody, IGN301 wherein the anti-idiotypic antibody produces a strong IgG response against Lewis-Y expressing epithelial cancer cells. The antibody is expressed in HEK293 cells, transformed human embryonic kidney cell cultures so would result in primate glycosylation.

It is not well established in the art that an antibody encompassed by the claims is amenable to the extent and degree of the modifications to the Fc or constant domain that would allow proper folding and assembly of the antibody, and the specification is not any more enabling for producing a functional, immunogenic antibody that meets all of the claim limitations.

b) Disclosure of drawings or structural chemical formulas: the specification and drawings do not show that applicant was in possession of the genus of immunogenic antibodies comprising an epitope or mimotope for a TAA much less where the antibody is hybridized to contain an IgG2a constant region and the constant region IgG1/IgG2a hybrid comprises any extent and amount of glycosylation.

c) Sufficient relevant identifying characteristics: the specification does not identify 1) a complete structure, ii) partial structure, iii) physical and/or chemical properties, or iv) functional characteristics coupled with correlation between structure and function for the genus of immunogenic antibody.

d) Method of making the claimed invention: the specification teaches making a single example of the hybrid immunogenic antibody in Figure 4 and Example 8.

e) Level of skill and knowledge in the art: the cloning of antibody DNA, construction Fc region hybrids, protein expression in CHO (hamster) and eukaryotic (primate cells) for hamster and primate glycosylation and bioassays for identifying functional regions within proteins was well established at the time of the invention.

f) Predictability in the Art: adequate written description for an antibody appears to depend upon whether the specification provides adequate written description for the antigen. While a specification may enable making a genus of antibodies, this does not necessarily place applicant in possession of the resultant antibodies (See *In re Kenneth Alonso* October (Fed. Cir. 2008) sustaining a lack of adequate written description rejection where "the specification teaches nothing about the structure, epitope characterization, binding affinity, specificity, or pharmacological properties common to the large family of antibodies" where the specification does not characterize the antigens to which the monoclonal antibodies must bind).

Applicants have not characterized the genus of IgG1/IgG2a hybrid antibody being hamster or primate glycosylated in the constant region and which renders or contributes to the immunogenicity of the antibody. Applicants have not characterized the

genus of epitopes or mimotopes comprising the immunogenic IgG1/IgG2a hybrid antibody and which confer immunogenicity for the antibody. The ordinary artisan could reasonably conclude that Applicants were not in possession of the claimed genus of immunogenic antibodies meeting all of the structural and functional requirements of the claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Debe et al. (U.S.A.N. 09/791,537; filed 2/22/01).

Claim 34 is interpreted as being drawn to the immunogenic recombinant antibody fragment comprising SEQ ID NO: 3 and hamster or primate glycosylation, and where as according to the instant specification a primate includes human.

According to the specification, the protein need only be immunogenic. Further and as according to Applicants admission on the record on p. 9 of the Response of 3/2/09, “the invention uses the antibodies as a "carrier" to deliver an antigen mimetic and/or immunogenic glycosylation” and therefore the antibody need not actually be functional or even contain the heavy and light chains.

The immunogenic antibody fragment was prima facie obvious at the time of the invention over Debe.

Debe discloses a protein sequence having 100% identity to the protein sequence of SEQ ID NO:3 (see attached sequence search alignment). Debe discloses the proteins being expressed from eukaryotic cells including CHO (Chinese Hamster Ovary) cells, NIH3T3, HEK293, and 3T3L1 cells (p. 25, line 12) and other mammalian host cells including CV-I (ATCC CCL 70), COS-1 (ATCC CRL 1650), COS-7 (ATCC CRL 1651), CHO-K1 (ATCC CRL 61), 3T3 (ATCC CRL 92), NIH/3T3 (ATCC CRL 1658), HeLa (ATCC CRL 2), C1271 (ATCC CRL 1616), BS-C-1 (ATCC CRl 26), AND MRC-5 (ATCC CCL 171) (p. 26, lines 10-13). Debe does not disclose the function of the protein but the same protein expressed in a hamster or primate cell, and thereby being hamster or primate glycosylated, would by inherency possess the property of being immunogenic in vivo. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. (See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989)).

Accordingly the ordinary artisan would have found motivation to isolate the protein of Debe from the CHO or primate cells in order to test the immunogenicity where Debe discloses identifying target structural motifs including epitopes (p. 15, lines 16-21) for the protein, and Debe teaches targeting antibodies against epitopes in the protein (p. 32, lines 19-20). The ordinary artisan would have been reasonably assured of success in identifying the immunogenicity of the protein because producing and testing for an immunogenic response against an administered protein was well within the skill of the ordinary artisan at the time of the invention. The immunogenic antibody fragment was prima facie obvious at the time of the invention.

## ***Conclusion***

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lynn A. Bristol/
Examiner, Art Unit 1643
Temporary Full Signatory Authority